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Case report

Primary renal tubular acidosis during pregnancy, what about the perinatal prognosis? A case report and literature review

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ABSTRACT

Renal tubular acidosis (RTA) is a group of disorders caused by tubular defects leading to defective reabsorption of bicarbonate (HCO_3^-) and/or secretion of protons (H^+). It is known that pregnancy can induce or worsen some forms of RTA. To date, no systematic data exist on the course of pregnancy in hereditary RTA-affected mothers, nor on the outcome of both mothers and children.

A 35-year-old female patient attends her routine obstetric follow-up consultation at 32-weeks' pregnancy. From the 6th week of gestation, she has been complaining of general malaise, accompanied by paraesthesia in both hands. She is known to have renal tubular acidosis type 1, carrying a mutation in the SLC4A1 gene encoding for the bicarbonate-chloride exchanger located in the alpha-intercalated cell of the renal collecting tubule. At week 32, serum bicarbonate levels appeared to be 11 mEq/l. The patient was hospitalised and treated with intravenous sodium bicarbonate and potassium chloride. After 5 days, the symptoms resolved, and her bicarbonate level had normalised. A healthy infant was born with a normal Apgar score. Carriage of the same mutation was found in the child at 16 months. Our literature study shows that 12 of the 13 reported infants born from a mother with primary RTA were healthy at delivery. One neonate revealed signs of hyperparathyroidism at day 2, but those signs resolved at 1 month of age.

RTA during pregnancy is often associated with decompensation and worsening of acidosis. More attention should be paid to patients with RTA suffering from hyperemesis gravidas, in particular regarding therapy adherence. Our literature review focusses on foetal prognosis, which seems to be favourable in most of the reported pregnancies.

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Acidosis tubular renal primaria durante el embarazo, ¿qué pasa con el pronóstico perinatal? Informe de un caso y revisión de la literatura

Palabras clave:
Acidosis tubular renal
Pronóstico perinatal
Acidemia
Suplementación de bicarbonato
Informe de caso

RESUMEN

La acidosis tubular renal (ATR) es un grupo de trastornos causados por defectos tubulares que causan la reabsorción defectuosa de bicarbonato (HCO3 –) y/o la secreción de protones (H+). Es sabido que el embarazo puede inducir o empeorar ciertas formas de ATR. Hasta la fecha no existen datos sistemáticos sobre el curso del embarazo en las madres afectadas por ATR hereditaria, ni tampoco en el resultado de madres e hijos.

Una paciente de 35 años acudió a consulta de seguimiento obstétrico rutinario a las 32 semanas de embarazo. Desde la 6ª semana de gestación se había quejado de malestar general, junto con parestesia en ambas manos. La paciente tenía acidosis tubular renal tipo 1, y portaba una mutación en el gen SLC4A1 que codifica el intercambiador de bicarbonato-cloruro localizado en la célula intercalada alfa del túbulo recolector renal. En la semana 32ª, los niveles de bicarbonato sérico se situaron en 11mEq/l. La paciente fue hospitalizada y tratada con bicarbonato sódico y cloruro potásico intravenosos. Transcurridos 5 días los síntomas se resolvieron, normalizándose su nivel de bicarbonato. Dio a luz a un bebé sano, con puntuación Apgar normal. Se encontró la misma mutación en el bebé, a los 16 meses. Nuestro estudio de la literatura muestra que 12 de entre 13 bebés reportados nacidos de una madre con ATR primaria fueron sanos en el parto. Un neonato reveló signos de hiperparatiroidismo el día 2°, pero dichos signos se resolvieron transcurrido un mes de edad.

La ATR durante el embarazo está asociada a menudo a una descompensación y empeoramiento de la acidosis. Deberá prestarse más atención a las pacientes con ATR que padecen hiperémesis gravídica, y en particular en lo relativo a la adherencia a la terapia. Nuestra revisión de la literatura se centra en el pronóstico fetal, que parece ser favorable en la mayoría de los embarazos reportados.

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Introduction

Renal tubular acidosis (RTA) is a group of disorders caused by tubular defects leading to defective reabsorption of bicarbonate (HCO_3^-) and/or secretion of protons (H^+).[1]

A pathophysiological distinction can be made into 4 types. Type 1 or distal RTA is the most frequent one characterised by a urinary pH higher than 5.5, due to impaired distal acidification. Type 1 RTA can be caused by primary gene defects, be secondary to autoimmune diseases or drugs, or can be classified as idiopathic.[2] On the contrary, type 2 or proximal RTA is seldom caused by a single gene defect. It is typically associated with a urinary pH that depends on serum bicarbonate levels. When bicarbonate levels exceed the renal reabsorption threshold, the urine becomes alkaline. However, when bicarbonate levels are lower, the urinary pH is generally below 5.5.[2,3] Type 3 RTA is caused by mutations in the gene encoding type II carbonic anhydrase, which acts in both the renal proximal and collecting tubule, covering patients presenting with both impairment of distal acidification and proximal reabsorption. Finally, Type 4 is a less frequent form of RTA associated with hyperkalaemia and hypoaldosteronism or aldosterone resistance.[4]

The most frequent presentation of type 1 RTA is a hyperchloremic acidotic state, accompanied by hypokalaemia and hypercalciuria with nephrocalcinosis, or nephrolithiasis. Patients can also present with osteoporosis. Depending on specific mutations in target genes, other specific symptoms can occur. For example, in cases of mutations in the SLC4A1 gene with autosomal dominant inheritance, a typical distal RTA presentation can occur. However, another mutation in the same gene with autosomal recessive inheritance can lead to different phenotypes, including a form of proximal RTA with glaucoma, cataract and keratopathy as main clinical features. Mutations in the ATP6V1B1 and ATP6V0A4 genes lead to a form of distal RTA associated with sensorineural hearing loss.[4]

It is known that pregnancy can induce or worsen some forms of RTA.[5,6] However, to our knowledge, few cases of RTA exacerbations during pregnancy have been reported. Transient presentations of idiopathic RTA have also been described during pregnancy. To date, the effects of chronic acidosis during pregnancy on foetal development and foetal prognosis have barely been studied. As noted by Seeger et al. (amongst others) no systematic data exist on the course of pregnancy in hereditary RTA-affected mothers, nor on the outcome of both mothers and children.[7]

Our paper presents the rare case of a woman with worsening of congenital RTA during pregnancy. A review of all reported cases of RTA exacerbations during pregnancy is done, with emphasis on foetal prognosis.

Case presentation

A 35-year-old female patient attends a routine obstetric follow-up consultation at 32-weeks' pregnancy. From the 6th

week of gestation, she has been complaining of palpitations, nausea, exercise intolerance, loss of appetite and tachypnoea, accompanied by paraesthesia in both hands in the morning. She has a healthy 12-year-old daughter and underwent an abortion because of trisomy 18 when she was 34. She was diagnosed with renal tubular acidosis type 1 (carrying a heterozygous dominant SLC4A1 mutation (c.1825G>A (p.(Gly609Arg), for which she is followed-up by a nephrologist.

The patient had initially been under nephrological follow-up since the age of 4.5 years, with biological signs of distal RTA presenting with alkaline urine (pH 7.2) but normal blood acidity during a screening test, along with an abnormal urine acidification test. However, for unknown reasons, her mother discontinued the citrate and bicarbonate supplementation. The genetic diagnosis of RTA type 1 was not made until she was 32 years old, after her mother's nephrologist encouraged her to resume follow-up. At that time, she was asymptomatic, and her potassium levels, urinary pH, and serum bicarbonate levels were 3.8 mmol/l, 7.37, and 26 mmol/l, respectively. No crystalluria was found. Kidney imaging revealed multiple bilateral non-obstructive nephrolithiases.

Her first pregnancy (when she was 28 years old) was characterised by hyperemesis gravidas until week 25 of gestation (lowest bicarbonate levels were 18 mEq/l, at week 36 of gestation).

Her family history includes RTA in her mother (with recurrent kidney stones and a chronic kidney injury stage 3) and maternal grandmother. Genetic investigation has never been performed for them. She has a healthy lifestyle (no smoking, no alcohol consumption). Her usual medication includes iron tablets and sodium bicarbonate 1000 mg tid. Ranitidine 300 mg once a day and meclozine 25 mg once a day were started during pregnancy because of pyrosis and nausea. At week 6 of gestation, the patient started experiencing hyperemesis for which intravenous rehydration with physiological solutes was given until week 8. Intravenous potassium was administered because of hypokalaemia (2.7 mEq/l) attributed to hyperemesis. The bicarbonate level was 17 mEq/l at this time (in comparison to a bicarbonate level of 26 mEq/l a few months before her pregnancy), with a plasma anion gap of 12 mEq/l and a urinary osmolar gap of 31 mEq/l. Her blood pressure remained normal (108/64 mmHg). As a result of loss of appetite, nausea and pyrosis, the patient had gradually stopped taking her sodium bicarbonate medication. Repeat ultrasounds revealed a steady foetal growth without structural defects nor arguments for placental dysfunction. When presenting at week 32, the patient was experiencing worsening tachypnoea and felt generally more unwell, with the presence of paraesthesia in both hands. A blood test was performed to rule out anaemia, and 'preoperative blood tests' were ordered, in preparation of an emergency Caesarean section. The bicarbonate levels appeared to be 11 mEq/l (with a potassium level of 3.2 mEq/l), which revealed a decompensated renal tubular acidosis. The patient was immediately hospitalised and treated with intravenous sodium bicarbonate and potassium chloride. After 5 days, her symptoms had resolved, and her bicarbonate level had normalised to 26 mEq/l. A peroral intake of sodium bicarbonate 3 g thrice a day was needed to maintain adequate serum concentrations during the rest of the pregnancy.

At week 39, labour was induced aiming at controlled delivery. When the membranes were pierced, some meconium was seen. A healthy infant weighing 3480 kg was born with an Apgar score of 10 at 1 and 5 min, without any sign of meconial aspiration. An arterial cord blood gas analysis was comforting, showing a slight respiratory acidosis (pH 7.16, pCO_2 56 mmHg, paO_2 38 mmHg, bicarbonate level 20 mmol/l). At the age of 18 months, the child started with sodium bicarbonate suppletion (1 g tid). At that time, he was at the 40th and 51st percentile for weight and height, respectively. His acid–base balance showed a serum bicarbonate level of 20 mmol/l. He had normocalciuria (2.7 mmol/l; 0.42 mg/mg creatinine) and no polyuria (0.96 ml/100 ml GFR). Carriage of the maternal SLC4A1 mutation had already been confirmed at the age of 16 months. He evolves perfectly, with adequate bicarbonate levels, normocalciuria and no evidence of kidney stones on echography at the age of five.

Discussion

The case was described of a woman with known autosomal dominant RTA type 1, presenting with severe metabolic acidosis during pregnancy. We will now perform a review of all published cases of decompensated primary RTA during pregnancy.

In a Pubmed-based literature study of all published cases, 11 cases of hospitalised women with primary RTA were found, accounting for 12 recorded pregnancies (Table 1).[7–14] Cases of secondary RTA during pregnancy were excluded as foetal and maternal prognosis is probably affected to a greater extent by the underlying cause than by the acidotic state in itself.

Three women had a proven congenital form of RTA, of whom 2 carried the ATP6V1B1 mutation and 1 carried the SLC4A1 mutation, like our patient. The SLC4A1 gene encodes the 'anion exchanger 1' protein, which is responsible for the exchange of bicarbonate with chloride in the basolateral membrane of kidney cells during the luminal secretion of hydrogen. The specific missense mutation (Gly609Arg) in the SLC4A1 gene described in our case report was previously identified as a cause of autosomal dominant distal RTA.

One woman was diagnosed with type 1 congenital RTA, however without proof of mutation analysis in the report.[11] Another patient experienced a sporadic transient form of RTA during pregnancy.[13] The other 6 women were classified as having an idiopathic form of RTA. In those cases, family history was not conclusive, mutation analysis was not reported, and secondary causes of RTA had been excluded. Congenital RTA could not be excluded with certainty in those cases.

Five out of the 11 patients were diagnosed with RTA during pregnancy. Virtually all patients were hospitalised with concomitant hypokalaemia (except patient 11 during her first pregnancy (Table 1,[14]). The most frequently identified symptoms and/or signs at presentation before a diagnosis was made were: hypokalaemia and muscle weakness, kidney stones, hyperemesis gravidarum and arterial hypertension, besides acidosis. Hypokalaemia and the ensuing muscle weakness can be explained by a compensatory loss of positively charged ions to maintain a normal acid–base state, and possibly also by a hyperaldosteronemic state.[5] Excessive renal loss of calcium

Table 1 – Reports of hospitalisation due to primary (congenital or idiopathic) RTA during pregnancy.

	Reference	Initial presentation at time of diagnosis	Pregnancy history (including described pregnancy)	Time of diagnosis (age/month (y/m) or pregnancy week (pw))	Type/mutation	HCO_3 (mEq/l) during pregnancy[a]	K^+ (mEq/l) during pregnancy[a]	Cl^- (mEq/l) during pregnancy[a]	Complications during gestation (except acidosis)	Peripartal complications	Outcome (infant)	Documented stop of alkali supplementation (yes/no/poor compliance)
Current patient	Van Laethem et al.	Asymptomatic, nephrocalcinosis diagnosed through screening;	G3P2A1 abortion: trisomy 18	Symptoms during pregnancy: pw 6	Type 1/SLC4A1	11	2.7	112	Hypokalemia, HG, hyperventilation	Meconium in amniotic fluid	Healthy at delivery	Yes
Patient 1	Hardarottir et al.	Nephrocalcinosis, muscle weakness	G2P2A0	18 y	Type 1/NM	12	2.8	112	Hypokalemia	Oligohydramnios	Healthy at delivery	No
Patient 2	Seeger et al.	Nephrocalcinosis, hearing loss	NM	4 m	distal RTA ATP6V1B1	15	3	128	Pyelonephritis, ureteral obstruction (JJ stenting)	None	Healthy at delivery	No
Patient 3	Seeger et al.	Nephrocalcinosis, hearing loss	G1P1A0	12 m	distal RTA; ATP6V1B1	21	3.3	108	HG	None	Healthy at delivery	Yes
Patient 4	Seeger et al.	Nephrocalcinosis, osteopenia	G4P3A1	18 m	SLC4A1	11	2.1	120	Hypokalemia, HG, HELLP syndrome, urinary tract infection	None	Healthy at delivery; failure to thrive, metabolic acidosis and nephrocalcinosis at 18 m	Yes
Patient 5	Alkhasoneh et al.	Muscle weakness, nausea	G3P2A1	Pw 32	Distal RTA; Idiopathic	6	2	113	Hypokalemia	None	Healthy at delivery	Yes
Patient 6	Becker et al.	Muscle weakness, nephrocalcinosis, polyuria and polydipsia, HG	NM	17 y	Idiopathic (no family history; mutation analysis did not exist at the time)	12	1	89	None	None	Healthy at delivery	No

– Table 1 (*Continued*)

	Reference	Initial presentation at time of diagnosis	Pregnancy history (including described pregnancy)	Time of diagnosis (age/month (y/m) or pregnancy week (pw))	Type/mutation	HCO_3 (mEq/l) during pregnancy[a]	K^+ (mEq/l) during pregnancy[a]	Cl^- (mEq/l) during pregnancy[a]	Complications during gestation (except acidosis)	Peripartal complications	Outcome (infant)	Documented stop of alkali supplementation (yes/no/poor compliance)
Patient 7	Savani et al.	Renal stones, rickets, bone fractures, secondary hyperparathyroidism, pyelonephritis	G5P4A1 1 stillborn Week 28, 1 infant died soon after delivery after 23 weeks gestation	Teenage years	Type 1/NM	14	NM	NM	Hypocalcemia, hyperparathyroidism	Preterm labour at week 36	Signs of hyperparathyroidism at day 2, but disappeared at 1 month	Poor compliance
Patient 8	Firmin	Muscle weakness, thirst, lethargy	G3P3A0 1 foetal loss soon after delivery (meconium aspiration), 1 intrauterine loss associated with polyhydramnios (w40)	Pw 30	Proximal RTA/NM	11	1.7	116	Hypokalemia	Induction of labour at week 38 due to history	Healthy at delivery and at 1 year	No
Patient 9	Srisuttayasathien et al.	Muscle weakness	G1P1A0	Pw 37	Idiopathic; transient during pregnancy	16	2	108	Hypokalemia, rhabdomyolisis, mild hydronephrosis	Caesarian section at 41w due to failure to progress	Healthy at delivery and at 6 weeks after delivery	NM
Patient 10	Rowe et al.	Arterial hypertension	G2P2A0	During first pregnancy (pw 35)	Type 1/NM	10	3.2	119	Arterial hypertension,hypokalemia	None	Healthy at delivery	NM
Patient 11 (first pregnancy)	Rowe et al.	Kidney stones	G4P2A2	10 y	Type 1/NM	23	3.8	115	Arterial hypertension	Spontaneous ruptured membranes at week 32	Healthy at delivery	NM
Patient 11 (second pregnancy)	Rowe et al.	Kidney stones	G4P2A2	10 y	Type 1/NM	14	3	114	Arterial hypertension	Labour induced at week 38 because of arterial hypertension	Healthy at delivery	NM

GPA: Gravida Para Abortus; HCO3: bicarbonate; K+: potassium; Cl-: Chloride; IV: intravenous; HG: hyperemesis gravidas; "healthy at delivery": no failure to thrive, normal Apgar score; HELLP: haemolysis, elevated liver tests and low platelets; NM: not mentioned; UTI: urinary tract infection; y: year(s); m: month(s); w: week(s).

[a] Lowest numbers are displayed for HCO_3^- and K^+, highest for Cl^-.

occurs based on the same mechanism, together with stimulation of osteoclastic activity in acid circumstances.[4] This can lead to secondary hyperparathyroidism, bone fractures, rickets (as in patient 7[11]) and the formation of kidney stones. Rowe et al. reported 3 pregnancies (patient 10–11) complicated by arterial hypertension, which can partially be explained by activation of the aldosterone-angiotensin system in response to the RTA associated volume contraction. Hypokalaemia and metabolic acidosis can induce or worsen hyperemesis gravidarum; both can also be induced or worsened by the latter. The associated nausea and hyperemesis will often lead to poor alkali and potassium adherence, which will in turn worsen the metabolic acidosis (despite the loss of HCl due to the vomiting) as well as hypokalaemia, sustaining a vicious circle.[5,7] Moreover, especially potassium citrate suppletion can cause gastrointestinal side effects, due to the irritative effect of the postassium component to the stomac lining. Therapeutic adherence could be enhanced by prescribing a new prolonged release formulation (ADV7103) in granules based on potassium citrate (1/3) and bicarbonate (2/3), which would be associated with lower rate of gastrointestinal discomfort.[15]

Our patient's nephrologist had hesitated whether to continue her sodium bicarbonate during pregnancy, since little is known about the effects of this medication on foetal development. However, it is known that renal tubular acidosis can worsen during pregnancy. Moreover, using common sense, administration of sodium-bicarbonate suppletion wouldn't be harmful, as sodium wouldn't lead to a pressor effect without chloride and pregnancy is a state where more sodium is required. Moreover, potential bicarbonate excess would only be excreted or exhaled. Bicarbonate concentrations drop during pregnancy for different reasons: increase in volume of distribution[5] and rise in glomerular filtration rate (GFR), sometimes up to 50%, lead to a higher bicarbonate clearance.[16] But most importantly, pregnancy hormone-induced respiratory alkalosis increases bicarbonate secretion.[17] After a discussion with the patient's obstetrician, the patient was given permission to continue her bicarbonate during pregnancy, but because of nausea and hyperemesis, oral bicarbonate was not continued.

In this literature review, it is striking to note that 5 out of the 12 patients (including ours) had interrupted their alkali intake, mostly due to hyperemesis. This highlights the fact that more attention should be paid to patients with RTA suffering from hyperemesis gravidarum, in particularly regarding therapy adherence. However, it is worth mentioning that continuation of alkali supletion does not guarantee a normal acid–base status during pregnancy: 2 out of 12 patients showed worsening of their acidosis despite the continuation of supplementary alkali[7,8] (Table 1). It would be rational to speculate that the patients with distal RTA would experience more severe acidaemia after discontinuation of alkali therapy than those with proximal RTA (where distal acidification is still intact). However, this cannot be proven due to the low patient number.

One of the most relevant questions for the caregivers and future parents is whether chronic acidosis, because of excessive bicarbonate loss or impeded tubular hydrogen secretion, is likely to harm the foetus. It seems obvious that the cause of the metabolic acidosis is a crucial factor to consider when looking at the foetal prognosis. Most reported RTA cases during pregnancy are due to toluene abuse, with high incidences of growth delay and foetal anomalies.[18,19] Other case reports of diabetic ketoacidosis during pregnancy showed an association with delayed neuro- and psychological development.[20,21] A high rate of other substance abuse was reported in the toluene group and it is unclear whether the ketosis and/or hyperglycaemic state led to negative outcomes in the ketoacidotic patients, rather than the acidosis itself. Hence, translation of these results to newborns from mothers with decompensated primary RTA is difficult. Bobrow et al. state that also the chronicity of the acidosis is a risk factor for poor foetal prognosis. His statement relies on 3 reports.[22] The first study shows a higher risk for unfavourable neonatal outcome in infants with intrapartum foetal asphyxia and metabolic acidosis compared to a similar group with respiratory acidosis. However, no case of chronic acidosis was included in this study.[23] In the second study, Nelson et al. found higher rates of antenatal events compared to peripartum events in patients with a history of cerebral palsy.[24] Yet, metabolic acidosis was not recorded as an antenatal event. Finally, Soothill et al. concluded that a lower blood pH after cordocentesis performed before labour in small for gestational age foetuses is associated with a significantly lower Griffiths's developmental quotient. Even so, the author mentions that it is very important not to extrapolate these results to foetal acidaemia associated with other conditions like RTA- and that a lower pH after cordocentesis should be seen as a result and as a marker of utero-placental dysfunction rather than as a cause of impaired brain development.[25]

Our literature study shows that 12 of the 13 infants born from a mother with primary RTA were healthy at delivery. One neonate (patient 7) had signs of hyperparathyroidism at day 2 (on wrist and mandibular X-ray), but these resolved at 1 month of age.[11] Another infant showed signs of failure to thrive, metabolic acidosis and nephrocalcinosis at 18 months of age.[7] However, the presence of the SLC4A1 mutation was found in this infant, which is a much more plausible explanation than any potential effect of chronic acidosis during gestation. Long-term follow-up information concerning these children is lacking, except for our case report. When looking at all viable pregnancies, including past pregnancies, 17 out of 22 pregnancies finally led to healthy newborns. Patient 7 delivered a stillborn at week 28 and a live born infant at week 23, who died a few days after birth. It is worth mentioning that this patient was known to have major symptoms of RTA and a poor therapeutic adherence (Table 1). Patient 8 suffered one newborn loss soon after delivery, associated with meconium aspiration and one intra-uterine loss associated with polyhydramnios at week 40. In this latter, the diagnosis of RTA was not yet made. In the aforementioned cases, it is difficult to conclude to fatal outcome due to chronic acidotic states in the mothers. Nonetheless, neither of the 2 patients were being treated nor followed-up for RTA at the time of their losses. In our described case, the child has little clinical expressivity of RTA up to now. This is expected, as in the autosomal dominant variant, patients are usually diagnosed later than in the autosomal recessive form, since the H^+ secretion pump function is initially intact.

To the knowledge of the authors, the data in Table 1 are the first of their kind, grouping all patient reports of primary RTA exacerbations during pregnancy. These data provide insight

into foetal prognosis in those patients, which seems to be relatively good in patients with adequate follow-up and timely treatment. However, due to the low patient number and the retrospective character of this literature study, our results should be validated in a prospective way and in a larger cohort of women. Moreover, it should be considered that there might also be a publication bias, with publication of the more severe cases.

Conclusion

We report the case of a pregnant patient hospitalised with severe metabolic acidosis, due to decompensation of primary RTA. It is known that pregnancy can exacerbate pre-existing RTA. Our literature review focusses on foetal prognosis, which seems to be favourable in most of the reported pregnancies. However, when looking at previous pregnancy histories of these patients, we cannot exclude that some foetal deaths could be linked to a state of chronic acidosis; further work is needed to investigate the impact of chronic foetal acidosis on foetal outcome. It is imperative to counsel women with primary RTA underlining the importance of therapeutic adherence during pregnancy. Close interdisciplinary follow-up by nephrologists and obstetricians should not be underestimated to prevent any possible complication of RTA in mother and child.

Authors' contributions

JVL is first author: study concept, data collection, data analysis and interpretation, writing and revision. LS, AT: study design, and revision. All authors have read and approved the manuscript.

Consent for publication

All included patients signed an informed consent form and agreed with any scientific publication.

Ethics

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

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Conflict of interest

The authors declare no conflict of interest.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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